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Attorney Docket No.: AVZ-007CP3

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

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Listing of Claims:

1. [Previously Presented] A method of increasing ATP production of a subject, comprising administering to said subject an effective amount of a creatine compound and an ATP enhancing agent, such that the ATP production is increased, wherein said creatine compound has the formula:

$$Z_{1}$$
 $C = X - A - Y$

and pharmaceutically acceptable salts thereof, wherein:

- Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, a) SO₃H, -C(=0)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight chain alkyl, C₂-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl;
- A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C5alkenyl, C2-C5alkynyl, and C1-C5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- K, where K is selected from the group consisting of: C_1 - C_6 1) straight alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

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-NH-M, wherein M is selected from the group consisting of: 3) hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;

- X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:
 - 1) hydrogen;
- K where K is selected from the group consisting of: C₁-C₆ straight 2) alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C3-C6 branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- a C5-C9 a-amino-w-methyl-w-adenosylcarboxylic acid attached 4) via the w-methyl carbon;
- a C5-C9 a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid 5) attached via the w-methyl carbon; and
- a C5-C9 a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R_2 is selected from the group consisting of:
 - 1) hydrogen;
- K, where K is selected from the group consisting of: C₁-C₆ straight 2) alkyl; C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6

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branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

- 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;
- B, wherein B is selected from the group consisting of: $-CO_2H$, -NHOH, $-SO_3H$, $-NO_2$, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl;
- straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P0₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and
- 7) -E, wherein E is selected from the group consisting of $(P0_3)_n$ NMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH_3)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of

connected by an amide linkage;

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the base; $-[P(=O)(OH)(CH_2)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C_1 , Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl; and if E is aryl, E may be

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- e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;
- f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and
- g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.
- 2. [Original] The method of claim 1, wherein said creatine compound is creatine.
- 3. [Original] The method of claim 1, wherein said creatine compound is cyclocreatine.
- 4. [Original] The method of claim 1, wherein said creatine compound is creatine phosphate.

Claim 5 (Cancelled).

- 6. [Previously Presented] The method of claim 1, wherein said ATP enhancing agent is a CoQ, spin trap, carnitine, antioxidant, vincopocetine or combination thereof.
- 7. [Original] The method of claim 6, wherein the agent is CoQ_{10} .
- 8. [Original] The method of claim 6, wherein the agent is carnitine.

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Claim 9 (Cancelled).

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10. [Original] The method of claim 6, wherein said antioxidant is pyruvate.

- The method of claim 6, wherein the antioxidant is lutein. 11. [Original]
- 12. [Original] The method of claim 6, wherein the agent is vinpocetine.
- The method of claim 1, further comprising administering a 13. [Original] herbal extract.
- 14. The method of claim 13, wherein the extract is rosemary or [Original] black caraway extract.
- 15. [Original] The method of claim 1, further comprising administering a berry oil or meal.
- 16. The method of claim 15, wherein said berry oil or meal is from [Original] blackberries, blueberries, black raspberries, or mixtures thereof.
- 17. [Original] The method of claim 1, wherein said subject is suffering or at risk of suffering from a nervous system disorder.
- The method of claim 1, wherein said subject is human. 18. [Original]

Claims 19-33 (Canceled).

34. [Previously Presented] A method of protecting the nervous system of a subject against oxidative damage, comprising administering to said subject an effective amount of a creatine compound and a neuroprotective agent, such that the nervous system of the subject is protected against oxidative damage, wherein said creatine compound has the formula:

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$$Z_1$$
 $C = X - A - Y$
 Z_2

and pharmaceutically acceptable salts thereof, wherein:

- Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(=0)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C1-C6 straight chain alkyl, C3-C6 branched alkyl, C2-C6 alkenyl, C3-C6 branched alkenyl, and aryl;
- A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂b) C5alkenyl, C2-C5alkynyl, and C1-C5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- 1) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and 2) contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
- 3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;
- X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, c) wherein R₁ is selected from the group consisting of:
 - 1) hydrogen;
- K where K is selected from the group consisting of: C₁-C₆ straight 2) alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C3-C6

branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

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- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- 5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
- 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;

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B, wherein B is selected from the group consisting of: $-CO_2H$, -NHOH, $-SO_3H$, $-NO_2$, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl;

- straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkyl, aryl and aroyl; and E is selected from the group consisting of:
 -(P0₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: Cl-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and
- 7) -E, wherein E is selected from the group consisting of (P0₃)_nNMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C₁, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;
- e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;

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f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

- g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.
- 35. [Original] The method of claim 34, wherein said creatine compound is creatine.
- 36. [Original] The method of claim 34, wherein said creatine compound is cyclocreatine.
- 37. [Original] The method of claim 34, wherein said creatine compound is creatine phosphate.
- 38. [Original] The method of claim 34, wherein said neuroprotective agent is an anti-oxidant compound.
- 39. [Original] The method of claim 38, wherein said antioxidant is selected from the group consisting of vitamin E, lutein, pyruvate, alpha-omega fatty acids, BHP, alpha-lipoate, thioctic acid, 1,2-dithiolane-3-pentanoic acid, 1,2-dithiolane-3 valeric acid, and 6,8-dithiooctanoic acid.

Claims 40-63 (Cancelled).

64. [Currently Amended] A method for treating amyotrophic lateral sclerosis in a subject, comprising:

administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that amyotrophic lateral sclerosis in said subject is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE

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inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:

$$Z_{1} C = X - A - Y$$

and pharmaceutically acceptable salts thereof, wherein:

- Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, a) SO₃H, -C(=0)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C1-C6 straight chain alkyl, C3-C6 branched alkyl, C2-C6 alkenyl, C3-C6 branched alkenyl, and aryl;
- A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C5alkenyl, C2-C5alkynyl, and C1-C5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- K, where K is selected from the group consisting of: C_1 - C_6 1) straight alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
- 3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;
- X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, c) wherein R₁ is selected from the group consisting of:
 - 1) hydrogen;

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2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

- 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- 5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
- 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;

B, wherein B is selected from the group consisting of: $-CO_2H$, -NHOH, $-SO_3H$, $-NO_2$, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl;

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- straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P0₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and
- -E, wherein E is selected from the group consisting of (P0₃)_nNMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C₁, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

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if R₁ and at least one R₂ group are present, R₁ may be connected by a e) single or double bond to an R2 group to form a cycle of 5 to 7 members;

- if two R₂ groups are present, they may be connected by a single or a f) double bond to form a cycle of 4 to 7 members; and
- if R₁ is present and Z₁ or Z₂ is selected from the group consisting of g) NHR2, -CH2R2 and -NR2OH, then R1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

Claims 65-68 (Cancelled).

69. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is a spin trap.

70. The method of claim 69, wherein said spin trap is [Previously Presented] PBN.

- 71. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is a cofactor for normal cellular metabolism.
- 72. [Previously Presented] The method of claim 71, wherein said cofactor is carnitine.
- 73. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is an antioxidant.
- 74. The method of claim 73, wherein said antioxidant is [Previously Presented] vitamin E.
- [Cancelled]. 75.
- 76. [Previously Presented] The method of claim 64, wherein said neuroprotective agent is riboflavin.

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77. [Previously Presented] The method of claim 64, further comprising administering at least one additional neuroprotective agent or creatine compound.

- 78. The method of claim 64, wherein said creatine [Previously Presented] compound is creatine.
- 79. [Previously Presented] The method of claim 64, wherein said creatine compound is creatine phosphate.
- 80. [Previously Presented] The method of claim 64, wherein said creatine compound is cyclocreatine.
- 81. [Previously Presented] The method of claim 64, wherein said creatine compound is cyclocreatine phosphate.
- 82. [Previously Presented] The method of claim 64, wherein said creatine compound is homocyclocreatine.

Claims 83-85 (Canceled).

86. [Currently Amended] A method for treating Parkinson's disease in a subject, comprising:

administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that Parkinson's disease in said subject is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:

$$Z_1$$
 Z_2
 $C = X - A - Y$

and pharmaceutically acceptable salts thereof, wherein:



a) Y is selected from the group consisting of: $-CO_2H$, -NHOH, $-NO_2$, $-SO_3H$, $-C(=0)NHSO_2J$ and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;

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- b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- 1) K, where K is selected from the group consisting of: C₁ -C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
- 3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;
- c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and

-COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

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- 4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- 5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
- 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;
- 5) B, wherein B is selected from the group consisting of: -CO₂H, -NHOH, -SO₃H, -NO₂, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl;

straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P0₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

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- 7) -E, wherein E is selected from the group consisting of $(P0_3)_nNMP$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; - $[P(=O)(OCH_3)(0)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; - $[P(=O)(OH)(CH_2)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C_1 , Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C_1 -C6 straight alkyl, C_2 -C6 straight alkenyl, C_1 -C6 straight alkoyl, C_3 -C6 branched alkyl, C_3 -C6 branched alkenyl, C_4 -C6 branched alkoyl; and if E is aryl, E may be connected by an amide linkage;
- e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;
- f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

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if R_1 is present and Z_1 or Z_2 is selected from the group consisting of g) NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

Claims 87-90 (Cancelled).

- The method of claim 86, wherein said 91. [Previously Presented] neuroprotective agent is a spin trap.
- The method of claim 91, wherein said spin trap is 92. [Previously Presented] PBN.
- 93. [Previously Presented] The method of claim 86, wherein said neuroprotective agent is a cofactor for normal cellular metabolism.
- 94. [Previously Presented] The method of claim 93, wherein said cofactor is carnitine.
- 95. [Previously Presented] The method of claim 86, wherein said neuroprotective agent is an antioxidant.
- [Previously Presented] 96. The method of claim 95, wherein said antioxidant is vitamin E.
- 97. [Cancelled]
- 98. [Previously Presented] The method of claim 86, wherein said neuroprotective agent is riboflavin.
- 99. [Previously Presented] The method of claim 86, further comprising administering at least one additional neuroprotective agent or creatine compound.
- 100. [Previously Presented] The method of claim 86, wherein said creatine compound is creatine.

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101. [Previously Presented] The method of claim 86, wherein said creatine compound is creatine phosphate.

102. [Previously Presented] The method of claim 86, wherein said creatine compound is cyclocreatine.

103. [Previously Presented] The method of claim 86, wherein said creatine compound is cyclocreatine phosphate.

104. [Previously Presented] The method of claim 86, wherein said creatine compound is homocyclocreatine.

Claims 105-107 (Canceled).

108. [Currently Amended] A method for treating Huntington's disease in a subject, comprising:

administering to a subject a therapeutically effective amount of a combination of creatine, a creatine phosphate or a creatine compound and a neuroprotective agent, such that Huntington's disease is treated, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, <u>2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10, wherein said creatine compound has the formula:</u>

$$Z_1$$
 $C = X - A - Y$
 Z_2

and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: $-CO_2H$, -NHOH, $-NO_2$, $-SO_3H$, $-C(=0)NHSO_2J$ and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

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- 1) K, where K is selected from the group consisting of: C₁ -C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
- 3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;
- c) X is selected from the group consisting of NR_1 , CHR_1 , CR_1 , O and S, wherein R_1 is selected from the group consisting of:
 - 1) hydrogen;
- 2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 4) a C_5 - C_9 a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

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- 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;
- B, wherein B is selected from the group consisting of: $-CO_2H$, -NHOH, $-SO_3H$, $-NO_2$, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl;
- 6) -D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P0₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q,

where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-[P(=O)(OH)(CH_2)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and $-CO_2G$, where G is independently selected from the group consisting of: Cl-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

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- -E, wherein E is selected from the group consisting of $(P0_3)_n$ NMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; - $[P(=O)(OCH_3)(0)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; - $[P(=O)(OH)(CH_2)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C₁, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;
- e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;
- f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and
- g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

Claims 109-112 (Cancelled).

113. [Previously Presented] The method of claim 108, wherein said neuroprotective agent is a spin trap.

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114. [Previously Presented] The method of claim 113, wherein said spin trap is PBN.

- 115. [Previously Presented] The method of claim 108, wherein said cofactor is a cofactor for normal cellular metabolism.
- 116. [Previously Presented] The method of claim 115, wherein said cofactor is carnitine.
- 117. [Previously Presented] The method of claim 108, wherein said neuroprotective agent is an antioxidant.
- 118. [Previously Presented] The method of claim 117, wherein said antioxidant is vitamin E.
- 119. [Cancelled].
- 120. [Previously Presented] The method of claim 117, wherein said neuroprotective agent is riboflavin.
- 121. [Previously Presented] The method of claim 108, further comprising administering at least one additional neuroprotective agent or creatine compound.
- 122. [Previously Presented] The method of claim 108, wherein said creatine compound is creatine.
- 123. [Previously Presented] The method of claim 108, wherein said creatine compound is creatine phosphate.
- 124. [Previously Presented] The method of claim 108, wherein said creatine compound is cyclocreatine.
- 125. [Previously Presented] The method of claim 108, wherein said creatine compound is cyclocreatine phosphate.

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126. [Previously Presented] The method of claim 108, wherein said creatine compound is homocyclocreatine.

Claim 127-129 (Canceled).

[Currently Amended] A pharmaceutical composition for treating amyotrophic 130. lateral sclerosis, Huntington's disease or Parkinson's disease in a subject, comprising a synergistically effective amount of a combination of a creatine compound having the formula

$$Z_{1} C = X - A - Y$$

$$Z_{2}$$

and pharmaceutically acceptable salts thereof, wherein:

- a) Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(=0)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C1-C6 straight chain alkyl, C3-C6 branched alkyl, C2-C6 alkenyl, C3-C6 branched alkenyl, and aryl;
- A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C5alkenyl, C2-C5alkynyl, and C1-C5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- K, where K is selected from the group consisting of: C₁ -C₆ 1) straight alkyl, C2-C6 straight alkenyl, C1-C6 straight alkoyl, C3-C6 branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 2) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;

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- c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- 5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
- 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl; C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6

branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

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- 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;
- B, wherein B is selected from the group consisting of: $-CO_2H$, -NHOH, $-SO_3H$, $-NO_2$, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1 - C_2 alkyl, C_2 alkenyl, and C_1 - C_2 alkoyl;
- straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P0₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and
- 7) -E, wherein E is selected from the group consisting of $(P0_3)_n$ NMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; - $[P(=O)(OCH_3)(0)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of

connected by an amide linkage;

the base; $-[P(=O)(OH)(CH_2)]_m$ -Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C_1 , Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, C_4 - C_6 branched alkoyl; and if E is aryl, E may be

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- e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;
- f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and
- g) if R₁ is present and Z₁ or Z₂ is selected from the group consisting of -NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z₁ or Z₂ to form a cycle of 4 to 7 members; and a neuroprotective agent and a pharmaceutically acceptable carrier, wherein said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, 2.3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10.
- 131. [Previously Presented] The pharmaceutical composition of claim 130, wherein said creatine compound is creatine.
- 132. [Currently Amended] A packaged composition, comprising a creatine compound having the formula

$$Z_{1}$$
C=X-A-Y

and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: $-CO_2H$, -NHOH, $-NO_2$, $-SO_3H$, $-C(=0)NHSO_2J$ and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;

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- b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:
- 1) K, where K is selected from the group consisting of: C₁ -C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
- 3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;
- c) X is selected from the group consisting of NR_1 , CHR_1 , CR_1 , O and S, wherein R_1 is selected from the group consisting of:
 - 1) hydrogen;
- 2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- 3) an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and

-COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

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- 4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- 5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
- 6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
- d) Z_1 and Z_2 are chosen independently from the group consisting of: =0, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z_1 and Z_2 may not both be =0 and wherein R₂ is selected from the group consisting of:
 - 1) hydrogen;
- 2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
- an aryl group, wherein the aryl group is a 1-2 ring carbocycle and contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
 - 4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;
- 5) B, wherein B is selected from the group consisting of: -CO₂H, -NHOH, -SO₃H, -NO₂, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C₁-C₂ alkyl, C₂ alkenyl, and C₁-C₂ alkoyl;

straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(P0₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁ -C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

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- 7) -E, wherein E is selected from the group consisting of (P0₃)_nNMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(0)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: C₁, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO=G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;
- e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;
- f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R₁ is present and Z₁ or Z₂ is selected from the group consisting of -NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z₁ or Z₂ to form a cycle of 4 to 7 members; and a neuroprotective agent, both packaged with instructions for using an effective amount of a combination of the creatine compound and said neuroprotective agent for the treatment of amyotrophic lateral sclerosis, Parkinson's disease or Huntington's disease, said neuroprotective agent is selected from the group consisting of inhibitors of glutamate excitotoxicity, 2,3 dimethoxy-5-methyl-6-decaprenyl benoquinone, nicotinamide, mitochondrial cofactors, electron transport chain regulators, spin traps, growth factors, nitric oxide synthase inhibitors, cyclooxygenase 2 inhibitors, aspirin, ICE inhibitors, neuroimmunophilis, N-acetylcysteine, antioxidants, lipoic acid, cofactors, riboflavin, and CoQ10.

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